A Comprehensive survey of on the use of food chemcials-generally recognized as safe (**GRAS**) 9/72

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A COMPREHENSIVE SURVEY OF INDUSTRY ON THE USE OF FOOD CHEMICALS GENERALLY RECOGNIZED AS SAFE (GRAS)

(Comprehensive GRAS Survey)

Subcommittee on Review of the GRAS List--Phase II

Committee on Food Protection

Food and Nutrition Board

Division of Biology and Agriculture

National Research Council

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NOTICE

The study reported herein was undertaken under the aegis of the National Research Council with the express approval of its Governing Board. Such approval indicated that the Board considered the problem to be of national significance; that its elucidation required scientific or technical competence and that the resources of NRC were particularly suitable to the conduct of the project. The institutional responsibilities of the NRC were then discharged in the following manner:

The members of the study committee were selected for their individual scholarly competence and judgment with due consideration for the balance and breadth of disciplines. Responsibility for all aspects of this report rests with the study committee, to whom we express our sincere appreciation.

Although reports are not submitted for approval to the Academy membership nor to the Council, each is reviewed according to procedures established and monitored by the Academy's Report Review Committee. Distribution of the report is approved, by the President, only after satisfactory completion of this review process.

PREFACE

In response to a directive in President Nixon's consumer message of 1969 concerning the need for reevaluation of safety of substances generally recognized as safe (GRAS), the Food and Drug Administration requested the National Academy of Sciences to develop and test a format and survey procedure that could be used to elicit information from industry on the extent of consumer exposure to the GRAS substances. Under terms of contract FD 70-22 Task Order 1, a special Subcommittee, under the general direction of the Committee on Food Protection, was appointed to carry out that assignment, which was reported (in December 1970) under the title "Development and Testing of a Survey Procedure for the Reevaluation of Safety of Substances Generally Recognized as Safe (GRAS Pilot Survey)." The Subcommittee's report on the pilot survey described the format and survey procedure developed, summarized the results of the testing of the procedure, and included recommendations and conclusions based upon the experience and results obtained.

Subsequently, the Food and Drug Administration requested the Academy to conduct the second phase of the program, i.e., a comprehensive survey of industry to determine the manner and extent of use of the GRAS substances in foods, employing the revised questionnaire and survey procedure developed in the pilot study. This assignment has been carried out by a new Subcommittee under terms of contract FD 70-22 Task Order 8 (modified by Supplemental Agreement dated June 6, 1972), as reported herein. [It should be noted that the Subcommittee's task was not to evaluate the safety of the GRAS substances, but rather to collect data from industry on the use of the substances in foods and to use the data obtained in estimating the consumer exposure to each substance on which reports were received.]

Subcommittee on Review of the
GRAS List--Phase II

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I. INTRODUCTION

This report is concerned not only with the NAS survey of GRAS substances, but also with the survey on flavoring ingredients and adjuncts conducted by the Flavor and Extract Manufacturers' Association and, in conjunction with them, by the National Association of Chewing Gum Manufacturers and the National Confectioners Educational and Scientific Foundation.

The main body of the report is comprised of 16 tables of data in computer printout form, together with 58 exhibits containing additional information and explanatory notes on the tables. The tables and exhibits are provided separately in the accompanying binders.

A complete listing of the tables is shown on pages 20-22, and of the exhibits on pages 39 and 40. The abbreviations and special terms used throughout the report are defined in Exhibit 1.

The 41 pages of discussion material, of which this page is one, serve to describe the methods and documents used in collecting and processing the data, and to provide commentary on the evaluation and interpretation of the data thus obtained.

II. SCOPE OF SURVEY

The following groups of substances were considered by the Subcommittee and by FDA to be included in the scope of the survey:

(1) Substances listed (as of July 1, 1970) in Code of Federal Regulations (CFR), Title 21, §121.101 (Subpart B);

(2) Substances covered by "prior sanction" issued before the effective date of the Food Additives Amendment under the Federal Food, Drug, and Cosmetic Act; and substances covered by the Poultry Products Act and the Meat Inspection Act;

(3) Substances published as materials generally recognized as safe by the Flavor and Extract Manufacturers' Association (FEMA);

(4) Substances considered to be generally recognized as safe on the basis of independent scientific judgment or the action of other responsible organizations;

(5) Substances covered by "no objection" letters issued by FDA after the Food Additives Amendment became effective; and

(6) Substances presumed to be GRAS by FDA but not published.

These categories were further defined by the Subcommittee as follows:

Category (1)--The primary GRAS list is comprised of substances cited in paragraphs (d), (e), and (g) of 21 CFR §121.101. Substances in paragraphs (e) and (g) were being included in a review of flavoring ingredients and adjuvants conducted by FEMA, as described below. Substances in paragraphs (f), (h), and (i) are either not used in human foods or are not added directly to human foods to perform some desired technical effect. Of the substances listed in 21 CFR §121.101, therefore, only those listed in paragraph (d) would be included in the NAS survey.

Category (2)--A number of substances were known to be permitted for use in foods under prior sanctions issued by FDA, although a listing of such substances could not be provided by FDA. Following the method used in the pilot survey (which elicited a number of reports on such substances), potential respondents would be informed that prior sanctioned substances were included in the scope of the survey, and such respondents would be requested to submit questionnaires on such substances that they use or

sell for use in food. Similarly, respondents would be requested to submit questionnaires on substances covered by the Poultry Products Act and by the Meat Inspection Act, although a listing of such substances would not be provided with the survey materials.

Category (3)--Both the Subcommittee and FDA were aware of a comprehensive review and survey of flavoring ingredients and adjuvants being conducted by FEMA and, in conjunction with them, by the National Association of Chewing Gum Manufacturers (NACGM) and the National Confectioners Educational and Scientific Foundation (NCESF). These surveys were designed to obtain data on the use of all flavoring materials and flavoring adjuncts used in the United States, including substances in §121.101(e), §121.101(g), §121.1163, and §121.1164; those declared GRAS by the FEMA Expert Panel; and other materials in use either by prior sanction or private determination of GRAS. The Subcommittee decided, therefore, that the NAS survey need not duplicate the coverage of the flavor surveys, but that the results of these joint efforts and the data so obtained would be tabulated and incorporated in the final NAS report.

Categories (4) and (5)--The Subcommittee had no information on substances in these two categories. Respondents in the NAS survey would be informed, however, that these substances were included in the scope of the survey and that questionnaires should be completed for them accordingly.

Category (6)--FDA provided a list of substances presumed to be GRAS but not published. This list would be included along with other lists in the group of NAS survey materials.

Summary of Scope

- The NAS survey would cover substances in 21 CFR §121.101(d) and substances presumed to be GRAS by FDA but not published. Potential respondents would also be asked to submit questionnaires on other substances not listed in the NAS survey, i.e., substances in Categories (2), (4), and (5) above.

- The FEMA survey would cover substances in 21 CFR §121.101(e), §121.101(g), §121.1163, and §121.1164; those declared GRAS by the FEMA Expert Panel; and other materials in use either by prior sanction or private determination of GRAS.
- The NACGM would conduct an independent survey of chewing gum manufacturers to obtain data on the use of GRAS substances and flavoring ingredients and adjuncts in chewing gum.
- The NCESF would conduct an independent survey of candy manufacturers to obtain data on the use of flavoring ingredients and adjuncts in highly flavored candy (principally hard candy, pressed mints, and drops).
- All of the data collected would ultimately be submitted to NAS for data processing and for inclusion in the Subcommittee's report to FDA.

III. SURVEY DOCUMENTS

The primary aim of the GRAS survey was to obtain information upon which the reevaluation of the safety of the GRAS substances could be made by FDA. To this end, the documents used in one or more of the surveys (NAS, FEMA, and subsurveys) were designed to obtain data of the following types for each substance:

- Food products to which the substance is added.
- Usual and maximum amounts of the substance added to each food product to achieve each intended technical effect.
- Technical effect achieved by use of the substance.
- Unpublished safety studies and bibliography of published reports.
- Number of pounds added to the nation's food supply annually and over the last decade.
- Extent to which each food processor relies on the substance to produce each intended technical effect (i.e., rating of importance).
- Year that the substance was first used in foods.
- Information on manufacturing process, composition, purity, and breakdown products formed during processing and storage.

Documents Used in NAS Survey

Covering letter (Exhibit 2, white paper)--This gave the potential respondent background information on the need for the reevaluation of the GRAS substances and explains the purpose of the NAS survey. Potential respondents were assured that the information provided on the questionnaires would be held confidential and that the data provided to NAS would be used only in overall tabulations in which individual responses and company identities would be merged and lost. The firms were also told that confidentiality of replies would be protected by the use of precoded forms in which the firms were identified only by randomly assigned code numbers.

Return Receipt (Exhibit 3, buff paper)--Each potential respondent was instructed to complete this form and return it to the GRAS Review Office upon receipt of the packet of survey material.

General Information (Exhibit 4, blue paper)--This section informed the potential respondents of the scope of the NAS survey and its relation to the FEMA and other subsurveys. It also explained the general content of the packet of survey materials and emphasized the confidential nature of the respondents' reports.

Survey Instructions (Exhibit 5, yellow paper)--This set of instructions explained in detail, in step-by-step fashion, the manner in which the questionnaire forms were to be completed. A slightly different set of Survey Instructions was used for reports on the use of GRAS substances in infant formula products and baby foods (Exhibit 6, yellow paper).

Questionnaire Form (Exhibit 7, white paper)--The NAS questionnaire was designed and precoded for automatic data processing by computer. One copy of the form was sent to each respondent. The individual company code number was inserted on each page of the form by the GRAS Review Office before the survey materials were distributed. The respondents were directed to use a separate form for each individual substance to be reported and to make as many photocopies of the blank form as required. A slightly modified form was used in obtaining information on usage levels in infant formula products and baby foods (Exhibit 8, white paper).

Appendix A (Exhibit 9, green paper)--This appendix consists of two parts: Part I (Sub. Nos. 0001-0251) is a listing of substances in 21 CFR §121.101(d); Part II (Sub. Nos. 0252-0334) is a listing of the substances presumed to be GRAS by FDA but not published. Substances in the appendix that are marked with an asterisk (principally flavoring adjuncts) were also included in the FEMA survey. [Note: Three substances were not included in Part I because they are restricted by 21 CFR §121.101(d) for use in animal feeds: glycine, methionine, and methionine hydroxy analogs.]

Appendix B (Exhibit 10, gold paper)--This is an expanded list of the abbreviated food category groups that were preprinted on the NAS questionnaire form for the report on usage levels (Question 8). Space was provided on the form for the respondents to specify additional food categories in those cases where the twenty-eight preprinted categories clearly did not fit the need. A different set of food category groups was used for infant formula products and baby foods (Exhibit 11, gold paper).

Appendix C (Exhibit 12, gray paper)--This is a listing of the technical effect groups that were precoded for use in connection with the usage level reports (Question 8). Respondents were directed to use the code number, as listed in the appendix, corresponding to the particular technical effect to be specified for each particular use within each food category in which the substance is used. The listing in the appendix was intentionally limited to a relatively small number of technical effects so that the respondents would not be confused by a long list of code numbers; this system had proved to be satisfactory in the pilot survey. As with the food categories, provision was made for the respondents to cite any technical effects not listed in the appendix.

Sample Questionnaire (Exhibit 13, pink paper)--This is a completed questionnaire in which hypothetical examples were used. It illustrates the style that the respondents were to follow in completing their individual questionnaires. A different sample questionnaire was used for infant formula products and baby foods (Exhibit 14, pink paper).

Documents Used in FEMA Survey

Covering Letter (Exhibit 15)--By means of this letter, FEMA advised the participants in the flavor survey of the need and significance for conducting the survey. The firms were advised that FEMA would take elaborate precautions to preserve the confidentiality of each firm's individual reply.

Transmittal Letter (Exhibit 16)--The questionnaires were transmitted with this brief accompanying letter.

Return Receipt (Exhibit 17)--The respondents were instructed to complete the receipt and return it to the FEMA office upon receiving the questionnaire.

Survey Instructions (Exhibit 18)--The instructions provided detailed information regarding the scope of the survey and its relation to the NAS survey and subsurveys on the use of flavoring materials in chewing gum and highly flavored candy. The instructions provided step-by-step procedures for completing the questionnaire, anticipating, to the extent feasible, the potential problems that might arise in providing the requested data. The participants were invited to supply any additional information they had regarding the surveyed or other similar substances.

Questionnaire (Exhibit 19, Sample Page Only)--The FEMA questionnaire consisted of a series of 129 identical pages on which the 1496 substances to be reported were preprinted, 12 per page. A complete list of the substances included in the FEMA questionnaire is provided in Table 1, Part B. [Note: A number of substances in the NAS survey (principally flavoring adjuncts) were also listed on the FEMA questionnaire; these substances are marked with an asterisk in NAS Appendix A, Exhibit 9.]

Documents Used in Subsurveys

The survey materials used to obtain data from the NACGM and NCESF on the use of flavoring ingredients and adjuncts in chewing gum and highly flavored candy, respectively, though differing in format, were similar in intent to those used in the NAS and FEMA surveys. Discussion of the format and execution of the subsurveys, provided by the respective organizations conducting the subsurveys, is presented in Exhibit 20 (chewing gum) and Exhibit 21 (highly flavored candy).

IV. SURVEY PROCEDURE AND PUBLICITY

Distribution of Questionnaires

Both the NAS and FEMA mailing lists were developed with the aid of a number of industrial trade organizations, as listed in Exhibit 22. The NAS and FEMA lists were almost identical in their coverage of food processors, but they differed with respect to manufacturers in that NAS concentrated on food chemical manufacturers and FEMA on flavoring ingredient manufacturers. The mailing lists used in the subsurveys on chewing gum and highly flavored candy were designed specifically to obtain information from virtually all U.S. manufacturers of products in these two commodity groups.

The NAS questionnaires were mailed during the week of July 15, 1971, to approximately 750 food processors, food ingredient suppliers, and food chemical manufacturers and distributors in the U.S. The FEMA questionnaires were sent to 785 firms on June 3, 1971. The subsurveys on chewing gum and highly flavored candy were conducted over a 16-month period, beginning in November, 1970.

Respondents in the NAS survey were requested to return their completed questionnaires according to the following schedule: substances in alphabetical group A through E by November 1, 1971; F through R by December 1, 1971; and S through Z by January 1, 1972. Respondents in the FEMA survey were asked to return their questionnaires by October 1, 1971. Those who did not respond by that date were contacted by letter so as to encourage a greater return of data. Respondents in the subsurveys were asked to return their questionnaires before the end of 1971, or as soon thereafter as possible.

As stipulated in the contract, the NAS mailing list (Exhibit 23) was submitted to FDA for review. FDA was given the opportunity to suggest additional firms to be added to the list. No additional names were proposed; instead, FDA issued a notice in the Federal Register (Vol. 36, No. 206--Saturday, October 23, 1971) to announce the GRAS survey publicly.

The notice (Exhibit 24) stated, in part:

> "There is no intent to overlook anyone who can supply information on the use of these substances. This notice is published for the purpose of announcing this survey and informing the public that the questionnaires were sent out beginning about July 15, 1971. If anyone who wishes to respond has not received a questionnaire within a reasonable time thereafter, he should request a questionnaire from the Subcommittee on GRAS Review, Food Protection Committee .... etc."

As a result of this notice, approximately 75 firms who had not been included on the NAS mailing list requested that the NAS questionnaire be sent to them.

Industry Publicity

In addition to the Federal Register notice, the GRAS survey was also publicized by special workshops and symposia arranged by a number of industry groups. One such workshop (Industry Briefing on the GRAS Questionnaire), held in New York City on May 27, 1971, was sponsored by 21 industrial associations (Exhibit 25). This workshop was attended by 314 persons representing approximately 242 firms.

A symposium sponsored by FEMA, held in Washington, D.C. on October 21, 1971, was attended by approximately 100 persons. The GRAS review was one of the major topics on the program (Exhibit 26).

The survey was also reported in a number of trade journals, association newsletters, and other news publications, e.g., Food Chemical News.

V. INDUSTRY RESPONSE TO SURVEY

Industry response to the overall GRAS survey (NAS, FEMA, and subsurveys) is shown in Exhibit 27. Detailed information on the extent of reporting on the individual substances is presented in Table 1, Parts A-D (see also explanatory notes in Exhibit 49).

The Subcommittee has estimated that the companies responding in the survey produce between 60 and 70% of the processed foods consumed in the United States (i.e., those foods to which the GRAS substances are added). These estimates are based upon data obtained from published financial reports (as incorporated in Standard and Poor's Register of Corporations, Directors, and Executives; Dun and Bradstreet's Million Dollar Index; and Moody's Handbook), upon statistics provided by trade associations, and upon food production figures obtained from government publications such as Bureau of the Census Annual Survey of Manufacturers, 1970 & 1971 Industry Profiles, M70 & M71.

VI. PROCESSING OF QUESTIONNAIRES AND CORRECTION OF RAW DATA

NAS Questionnaires

Respondents in the NAS survey mailed their completed questionnaires directly to the NAS GRAS Review Office. All attachments to the questionnaires submitted in response to the following questions were removed and transmitted to FDA without review by the Subcommittee (only after company code numbers were removed or obliterated): (a) specifications of identity and purity; (b) further information on composition; (c) known effects of processing and storage; (d) unpublished data on safety; (e) bibliography of published reports; and (f) manufacturing process. The attachments corresponded to information requested on page 2 of the NAS questionnaire (i.e., boxes 36-50 and 55-61).

The NAS questionnaires were subjected to rigorous manual checks during coding to determine if the respondents had committed any obvious errors in completing the forms (i.e., substance number not matching substance name; substance number not entered on one or more pages of the questionnaire; incorrect technical effect codes listed; etc.). In those cases in which the respondent's intended entry was clearly obvious, the incorrect entry was corrected by the NAS GRAS Review Office; in those cases in which the intention was not obvious, the respondent was later contacted and asked to clarify his response. [Note: A number of food category designations were later changed as explained in Exhibit 33A.]

After keypunching, the data were transferred to magnetic tape and subjected to computer edit to detect keypunch errors and any additional respondent errors not uncovered during the coding phase. These errors were corrected as described above.

A listing of all usage level reports on substances used in regular foods was subsequently printed out. Following a brief review of this listing, it was apparent that many respondents had reported their usage levels incorrectly, almost invariably on the high side.

The chief reason for such incorrect reporting was that the respondents had not followed the Survey Instructions (Exhibit 5) concerning reports on the levels used in the final foods as consumed. Respondents often reported the usage levels on the basis of the concentration of the substance added to dry mixes, concentrated bases, or other intermediate products, rather than on the basis of the levels occurring in the final foods as consumed, after mixing with water or dilution with other ingredients.

The detection of such possibly erroneous reports was greatly facilitated by the information contained in the section in Question 8 (Usage Levels, boxes 29-42) entitled "Specific Food in Which Maximum Level Used" (see pp. 3-6 in the Questionnaire, Exhibit 7). In this column respondents had often indicated "Dry Mix", "Bev Concentrate", "Instant Mix", etc. Consequently, the computer was programmed to print out for each firm any and all reports in which the Specific Food had been indicated as being "Dry", "Concentrate", "Instant", "Mix", "Dehydrated", etc. The printouts were mailed to each of 80 firms, who were instructed to correct the usage levels to show the concentrations of the GRAS substances in the foods as consumed (Exhibit 28). All 80 firms returned the printouts; approximately 75% corrected their usage levels, and the other 25% indicated that the data were correct as originally reported.

Further review of the original listing revealed that a number of reported usage levels were still suspect, and many were obviously incorrect. For example, one firm reported that sodium bisulfite was used in food category 14 (vegetable products) as a potato whitener at a usual level of 99.0%; obviously, the firm wished to indicate that the potato whitener was 99.0% pure sodium bisulfite, not that 99.0% of the potato product itself consisted of sodium bisulfite. In reporting on chemical processing aids or modifying agents (e.g., starch modifiers), several firms reported the levels of the chemicals used in processing, not the residual levels occurring in the finished food products (also see discussion in Chapter X).

A second computer printout of such reports (or of as many such reports as could be detected by visual inspection of the data) was prepared and mailed to another 21 firms, the majority of whom subsequently corrected their usage levels to the basis of actual or estimated concentrations of the GRAS substances in the finished foods as consumed.

In those few cases in which respondents did not submit corrected usage levels, or did not confirm that their levels as originally reported were correct, or in which the usage levels were still questionable after the respondents confirmed that they were valid, such data were withheld from further processing and were not used in subsequent calculations. These cases represented only 0.18% of the total number of reports submitted to NAS on regular foods.

A separate listing was printed out on the use of GRAS substances in infant formula products and baby foods. Again, it was apparent that many of the respondents had reported their levels on the dry or undiluted basis. Rather than sending the firms data to review on selected usage level reports, as was the case for regular foods described above, it was decided that each firm should be sent all of his reports for review and correction as necessary (see Exhibit 29). Approximately half of the 14 firms found it necessary to correct their usage levels, the other half indicating that their data were correct as originally submitted. In the latter cases, the data were processed as originally submitted by the respondents.

FEMA Questionnaires

The FEMA questionnaires were received first in the FEMA office, where they were subjected to a careful review to determine if the respondents had committed any obvious errors or made omissions in completing the forms. As a consequence of this review, 162 respondents were requested, in writing, to confirm or correct the information submitted in the survey.

After keypunching by NAS, the data were transferred to magnetic tape and subjected to computer edit as described above for the NAS data.

An unedited printout of all usage level data submitted on each substance was reviewed by a subcommittee of expert flavor chemists (see listing in Exhibit 30) of the FEMA Food Additives Committee. As with the NAS data, many of the FEMA usage levels were suspected of having been reported incorrectly; again, most of the suspect reports appeared to have been on the high side. Since virtually all such levels would have been organoleptically intolerable by the consumer, it was obvious that such levels had been reported on the dry or undiluted basis of premixes, such as gravy or drink mixes (see also discussion in Chapter X).

Computer printouts of the suspect data were subsequently prepared and sent to approximately 80 firms, who were asked to review the data and to advise FEMA of the correct values (Exhibit 31). After the responses of the firms that replied were tabulated, a small residue of questionable values, amounting to approximately 0.2% of the total data supplied in the FEMA survey, remained. These values, which were regarded as errors, or as outside the limits of good manufacturing practice, were excluded from further processing and the firms were so notified.

Subsurvey Questionnaires

All usage levels and other data obtained in the chewing gum and highly flavored candy subsurveys were verified and corrected by the respective subsurvey organizations before being submitted to NAS for processing.

VII. CLASSIFICATION OF DATA

The data received from all respondents in the NAS and FEMA surveys and in the subsurveys on chewing gum and highly flavored candy were ultimately combined for data processing into five major groups as shown below:

Group I--Data on substances in NAS Appendix A (Parts I and II) reported as being used in regular foods. This group is comprised of reports on NAS Sub. Nos. 0001-0334 obtained from all sources: (1) NAS questionnaires, (2) FEMA questionnaires, (3) chewing gum and highly flavored candy subsurveys, and (4) additional reports to FEMA on such substances.

Group II--Data on substances in NAS Appendix A (Parts I and II) reported as being used in infant formula products and baby foods. This group is comprised of reports on NAS Sub. Nos. 0001-0334 made to NAS via the NAS infant formula product and baby food questionnaires only.

Group III--Data on FEMA questionnaire substances not listed in NAS Appendix A. This group is comprised primarily of reports on flavoring ingredients obtained directly from the FEMA questionnaires and from the chewing gum and highly flavored candy subsurveys, but a few reports to NAS on such substances are also included.* The substances are subgrouped as follows:

A. 21 CFR §121.101(e)
B. 21 CFR §121.101(g)
C. 21 CFR §121.1163
D. 21 CFR §121.1164
E. FEMA substances not included in A-D above but listed in FEMA's GRAS lists 3, 4, and 5 (as published in Food Technology)
F. Other substances listed in FEMA questionnaire but not included in A-E above.

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*NAS respondents reported the use of two Group III substances (DL-methionine and orange oil) in infant formula products and baby foods. These data have been placed in Group IV, rather than Group III, inasmuch as the Group III data are not otherwise used in calculating daily intakes from consumption of infant formula products and baby foods.

Group IV--Data on substances not listed in NAS Appendix A or in the FEMA questionnaire. This group is comprised of additional reports to NAS and FEMA on substances that are not included in Groups I-III. Reports on the use of such additional substances in both regular foods and in infant formula products and baby foods are included in this group.*

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* Same footnote as on page 16.

VIII. USE OF SURVEY DATA AND PROCUREMENT OF SECONDARY DATA

Survey Data

The data submitted by all user firms (NAS, FEMA, and subsurveys) were ultimately used to estimate the daily intake of those substances listed in NAS Appendix A and in the FEMA questionnaire on which usage levels were reported. To calculate such intakes required not only usage level data (by individual food categories) but also data on the amounts of foods consumed per food category. Data on food consumption were not obtained in any of the surveys described herein. However, the NAS-FDA contract provided for the purchase of a portion of the required information from a commercial source, the Market Research Corporation of America (MRCA). In addition, a computer tape containing data from the U.S. Department of Agriculture's survey on food intake and nutritive value of diets of men, women, and children in the United States, Spring 1965, was supplied gratis to the Subcommittee.

MRCA Data

MRCA's Third National Household Menu Census, conducted in 1967-68, determined the eating habits of 4,000 families (12,857 individuals), with each family participating for 14 consecutive days (see Exhibit 32A). The sample selection was controlled by family size, age of housewife, city size, region, and income group, thus achieving a statistically representative cross-section of all U.S. households in 48 states (excluding Alaska and Hawaii). By the end of the census period in June 1968, over 250,000 family meals and 750,000 personal meals (both in-home and away-from-home), involving a total of 3,000,000 food items, were recorded.

The MRCA data were collected in terms of the number of times each food item was eaten per individual during a 14-day period; however, the amounts of food consumed were not included in the census and thus were not recorded. To utilize the MRCA data in calculating food consumption per food category required the procurement of additional data on the mean portion size of foods consumed in each food category. This information was obtained from the USDA food intake survey.

USDA Data

The 1965 USDA survey determined the daily food intake of a representative sample of 14,500 men, women, and children (approximately 6,200 households) in the United States. Information on the amounts of foods eaten was obtained by the recall method for the day preceding the interview. Data were collected for all days of the week. Additional information on the USDA survey is provided in Exhibit 32B.

Although food consumption values, on a one-day basis only, could have been obtained from the USDA data alone, the Subcommittee believed that the more recent 14-day MRCA census would provide more statistically significant information on individual eating habits. It was decided, therefore, that the USDA data would be used primarily to obtain information on the mean portion size of each food consumed.

Summary

Food consumption values for each food category were derived from the MRCA data on frequency of eating (Exhibits 34-38) and from the USDA data on mean portion size of foods in each food category (Exhibits 39-41). The food consumption values thus derived (Exhibits 42-48) were coupled with the usage level data obtained in the surveys (Tables 2-5) to calculate the daily intake of each substance. Intakes of substances in Groups I and II are shown in Table 13, Part A (total dietary), and in Table 14, Part A (individual food category). Intakes of substances in Group III are shown in Table 13, Part B (total dietary), and in Table 14, Part B (individual food category). Finally, intakes of substances in Group IV, on an individual food category basis only, are shown in Table 15.

IX. PRESENTATION OF SURVEY DATA (LISTING OF TABLES)

All tables listed in this chapter are presented in computer printout form, provided in separate binders accompanying this report. Explanatory notes on the tables are included in the Exhibits section, also provided in separate binders.

Reports Submitted on Survey Substances [See Notes in Exhibit 49]

Table 1, Part A--Reports Submitted to NAS on Substances Listed in NAS Appendix A, Parts I & II

Table 1, Part B--Reports Submitted to FEMA on Substances Listed in FEMA Questionnaire

Table 1, Part C--Reports Submitted to NAS on Additional Substances (Not Listed in NAS Appendix A)

Table 1, Part D--Reports Submitted to FEMA on Additional Substances (Not Listed in FEMA Questionnaire)

Usage Levels [See Notes in Exhibit 50]

Table 2--Usage Levels Reported for NAS Appendix A Substances (Group I*) Used in Regular Foods

Table 3--Usage Levels Reported for NAS Appendix A Substances (Group II) Used in Infant Formula Products & Baby Foods

Table 4--Usage Levels Reported for FEMA Questionnaire Substances Not in NAS Appendix A (Group III)--Regular Foods Only

Table 5--Usage Levels Reported for Additional NAS & FEMA Substances (Group IV)

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*The classification of the substances into Groups I, II, III, and IV is described in Chapter VII.

Technical Effects and Importance Ratings [See Notes in Exhibit 51]

Table 6--Technical Effects and Importance Ratings for NAS Appendix A Substances Used in Regular Foods (Group I)

Table 7--Technical Effects and Importance Ratings for NAS Appendix A Substances Used in Infant Formula Products and Baby Foods (Group II)

Table 8--Technical Effects/Flavor Uses and Importance Ratings for FEMA Questionnaire Substances Not Listed in NAS Appendix A (Group III)

Table 9--Technical Effects/Flavor Uses and Importance Ratings for Additional NAS and FEMA Substances (Group IV)

Table 10--Substances Used for Each Technical Effect Within Each Food Category (Groups I-IV)

Annual Poundage [See Notes in Exhibit 52]

Table 11, Part A--Annual Poundage Data for NAS Appendix A Substances (Groups I and II)

Table 11, Part B--Annual Poundage Data for NAS Appendix A Substances (Groups I and II) Ranked by Total 1970 Poundage Reported

Table 11, Part C--Annual Poundage Data for FEMA Questionnaire Substances Not Listed in NAS Appendix A (Group III) -- 1970 Data Only

Table 11, Part D--Annual Poundage Data for FEMA Questionnaire Substances Not Listed in NAS Appendix A (Group III) Ranked by Total 1970 Poundage Reported

Year of First Use [See Notes in Exhibit 53]

Table 12--Year of First Use Data for NAS Appendix A Substances (Groups I and II) Submitted by NAS Respondents Only

Daily Intakes Per Food Category and Total Dietary [See Notes in Exhibit 54]

Table 13, Part A--Possible Daily Intakes of NAS Appendix A Substances (Groups I and II), Per Food Category and Total Dietary, Based on Food Consumption by Total Sample

Table 13, Part B--Possible Daily Intakes of FEMA Questionnaire Substances Not in NAS Appendix A (Group III), Per Food Category and Total Dietary, Based on Food Consumption by Total Sample

Daily Intakes Per Food Category Only [See Notes in Exhibit 55]

Table 14, Part A--Potential Daily Intakes of NAS Appendix A Substances (Groups I and II), Per Food Category, Based on Food Consumption by Eaters Only

Table 14, Part B--Potential Daily Intakes of FEMA Questionnaire Substances Not Listed in NAS Appendix A (Group III), Per Food Category, Based on Food Consumption by Eaters Only

Table 15--Potential Daily Intakes of Additional NAS and FEMA Substances (Group IV) Per Food Category Reported, Based on Food Consumption by Eaters Only

Ranking of Substances by Intake [See Notes in Exhibit 56]

Table 16--All NAS Appendix A and FEMA Questionnaire Substances (Groups I, II, and III) Ranked by Possible Average Daily Intake

Part A--Intake by 0-5 Months, Total Sample

Part B--Intake by 6-11 Months, Total Sample

Part C--Intake by 12-23 Months, Total Sample

Part D--Intake by 2-65+ Years, Total Sample

X. CRITIQUE OF DATA

Reports Submitted on Survey Substances (Table 1, Parts A-D)

The data in this table summarize the various types of information submitted by the survey respondents on each substance.

Usage Levels (Tables 2-5)

The NAS Subcommittee has assessed the usage level data on substances reported to NAS, as presented in these tables. Similarly, the usage level data on flavoring ingredients and adjuncts reported to FEMA, as presented in these tables, have been assessed by a subcommittee of expert flavor chemists of the FEMA Food Additives Committee and, when reported in the subsurveys, by the respective organizations conducting the subsurveys on chewing gum and highly flavored candy.

It has been concluded that the levels shown in Tables 2-5, with certain exceptions (see below), appear to be reasonably accurate and that they are indicative of the concentrations of the substances currently being added to foods (but not necessarily surviving into the final foods) processed in the United States. In reaching this conclusion, the NAS Subcommittee endorsed the findings of the FEMA subcommittee and the subsurvey organizations with respect to the accuracy of the data and extent of reportage on flavoring ingredients and adjuncts used in regular foods, chewing gum, and highly flavored candy. (In both the NAS and FEMA surveys, a limited number of reports believed to have been clearly erroneous were withheld from processing if corrected usage levels could not be obtained from the respondents; see discussion on this point in Chapter VI.)

The exceptions mentioned above are as follows:

- The use of many substances in a particular food category was often reported by only 1, 2, or 3 firms (indicated by the asterisk in the tables as explained in Exhibit 50). Evidence of such limited use should be taken into consideration in utilizing the estimated total dietary intakes of these substances, as discussed in Chapter XI.
- Although most substances are used at relatively low levels in the various food categories, a few substances are used as the major component of speciality products in certain categories. In these cases, the mean usage levels are greatly influenced by these exceptionally high uses, and they often do not accurately reflect the overall use of the substance in the particular food category. Outstanding examples (see Table 2) are the use of gum acacia (NAS 0001) in soft candy; caramel (NAS 0059) in gravies and sauces; monosodium glutamate (NAS 0134) in seasonings and flavors; and sorbitol (NAS 0212) in soft candy. In these examples, the weighted means of the usual levels are from approximately 9 to over 300 times greater than the median of the usage levels reported for these substances in these particular food categories.
- A slightly different example, incorporating the exaggerated effects cited in both of the two preceding discussions, is the case in which only 1, 2, or 3 firms reported on the use of a substance that is the major component of a specialty product in a single food category. An example of this type (see Table 2) would be the use of mannitol (NAS 0126) in soft (dietetic) candy. When such uses are reported, the weighted mean itself may not be seriously affected (and would not be when only one firm is reporting), but the effect is that the apparent use of the substance, and consequently the estimated daily intake, is greatly overstated.

- The levels reported for gaseous, volatile, and labile substances, including a number of solvents and flavoring agents, may not and usually do not represent the concentrations of the substances at the time the food is consumed. Examples are benzoyl peroxide (NAS 0254), carbon dioxide (NAS 0060), hydrogen peroxide (NAS 0098), and sulfur dioxide (NAS 0217-FEMA 3044) in Table 2; ethyl alcohol (FEMA 2419E-NAS 0377) and ethylene oxide (FEMA 2433E) plus numerous flavoring agents in Table 4; and acetone (FEMA 3588) in Table 5.
- Levels shown for the enzymes may not represent the residual concentrations occurring in the food products after processing and packaging. For example, enzyme activity does not remain at the level of addition to unpasteurized malt beverages and continues to decline after packaging. Moreover, enzymes are deactivated in products that are pasteurized. [Note: Further comments submitted by the United States Brewer's Association regarding the use of GRAS substances employed in the brewing of malt beverages are shown in Exhibit 57.]

The following additional comments regarding the usage level data should be noted:

- Although nonuser firms, as distinguished from user firms (see definition in Exhibit 1), were given an opportunity in the GRAS survey to submit data on the levels that they recommend be used in food processing, most nonuser firms submitted only token data. Furthermore, the usage level data that were submitted by nonuser firms were considered to be much less reliable than the data reported by the actual users. Consequently, only the data reported by user firms were used in calculating daily intakes of the GRAS substances. (It should be noted, however, that the nonuser firms -- principally suppliers of the basic materials -- submitted proportionately more unpublished data on safety studies and more bibliographies than did the user firms.)

- As explained in Exhibit 50, Note 8, the usage levels were weighted according to the 1970 annual poundage data reported by each firm. The Subcommittee believes that the weighted means give a more accurate indication of the levels of the substances added to the nation's food supply than would simple unweighted means in which each firm's usage levels would have counted the same, regardless of the poundage of the substance used.
- Many substances for which alternatives are available are used at a lower level, if at all, than they would be used in the absence of alternatives. This applies particularly where substances with the same technical effect (see Table 10) are used in combination.

Technical Effects and Importance Ratings (Tables 6-10)

The technical effects cited in these tables have not been critically evaluated by the Subcommittee. Except in a few cases where obvious errors in reporting were corrected, the technical effects appear as they were originally reported by the respondents.

The importance ratings in Tables 6-9 are recorded exactly as reported by respondents and have not been reviewed by the NAS Subcommittee, by FEMA, or by the subsurvey organizations. Since the importance ratings merely reflect the extent to which the food processors rely upon each substance to impart its intended technical effect, a review of the respondents' ratings was not indicated. The Subcommittee, however, does wish to call attention to some of the views expressed in this connection by participants in the NAS pilot survey, as to the practical possibility of replacing a substance, in whole or in part, by any available alternatives for each of its various applications. If there were satisfactory and currently available alternatives, the substance would rate a "C." If the alternative(s) were to be eliminated or were of doubtful acceptability, the rating would become a "B" or an "A."

Annual Poundage (Table 11, Parts A-D)

Although the NAS and FEMA questionnaires were not sent to all of the tens of thousands of U.S. food processors (the great majority is comprised of local bakeries, dairies, and canners), the Subcommittee has estimated that the respondents in the GRAS survey (NAS + FEMA + subsurveys) produce between 60 and 70% of the regular foods (and at least 90% of the infant formula products and baby foods) processed for consumption in the United States. In addition, the subsurveys on chewing gum and highly flavored candy covered at least 90% of the manufacturers of these products. Thus, the annual poundage data reported by all respondents is estimated to represent between 60 and 70% of the actual poundage of the GRAS substances added to the nation's food supply annually (see discussion in Chapter V and further explanations in Exhibit 52).

[Note: Annual poundage data are not presented for additional nonflavor substances or additional flavoring ingredients (i.e., substances in Group IV), because these substances were not listed in any of the questionnaires and very few reports were submitted on them, usually just one or two firms per substance. If the substances had been listed in the questionnaires, more reports on certain substances may have been submitted by additional firms. The Subcommittee believes, therefore, that to present any annual poundage data on these substances would not only be misleading but would also not serve any useful purpose in even partially indicating the overall usage of the substances. Furthermore, many of the substances, in the conventional sense, would be more properly regarded as foods (applesauce, bananas, honey, etc.) rather than as food additives.]

Year of First Use (Table 12)

The data in this table are those obtained from NAS respondents who reported on NAS Appendix A substances used in regular foods (Group I) and in infant formula products and baby foods (Group II). Although data on year of first use were submitted on flavoring ingredients used in chewing gum, this question was not included in the FEMA questionnaire itself; therefore, year of first use data are not presented for flavoring ingredients listed in the FEMA questionnaire (i.e., substances in Group III).

Data are not presented for substances in Group IV for the same reasons mentioned in the discussion of Annual Poundage.

The Subcommittee has made no attempt to assess or evaluate the data on year of first use presented in Table 12, since the data are recorded exactly as reported by respondents and are self-explanatory.

Daily Intakes (Tables 13-16)

General Comments

The validity of the data in Tables 13-16 depends entirely on the validity of the usage level and food consumption data from which the intakes were calculated.

As noted earlier, the Subcommittee found the usage level data to be reasonably accurate, but with certain exceptions as listed on pp. 24 and 25. The intakes in Tables 13-16, therefore, should be viewed in light of the Subcommittee's discussion of these exceptions. This point is discussed further in Chapter XI.

The food consumption data presented in Exhibits 42-47 are believed to be as accurate as can be derived from the information currently available. The following points should be noted:

- For the purpose of this survey, the data were based on a wide variety of commercial food products, rather than on the more conventional food groups ordinarily used in nutrition studies and surveys.
- For some food categories, the number of persons in either the MRCA or USDA survey populations, or both, was fewer than ideal. Furthermore, some food categories on which data were required were not included in the USDA survey, or the data available were completely inadequate for statistical use; in these cases, the Subcommittee made estimates of the mean portion sizes of the food categories involved. Despite these deficiencies, the Subcommittee believes that the overall data on food consumption (as presented in Exhibits 42-47 and as explained in further detail in Exhibit 48) are satisfactory for the purposes of this survey. However, closer estimates of daily intakes could have been made if better food consumption data had been available or could have been derived from the existing information.

- Although consumption values were computed for unprocessed as well as processed foods, data on the former were not used in calculating daily intakes inasmuch as these foods would not be expected to contain any of the substances (other than those occurring naturally) reported herein (see further discussion in Exhibit 33A, Note 3).

- Consumption data were obtained for infant formula products and baby foods as well as for regular foods.
- Data on frequency of eating, from which the food consumption values were calculated, were obtained on foods eaten away from home as well as in the home.
- The mean food consumption values were derived from the USDA mean portion size data and the MRCA mean frequency of eating data; high values were obtained from the USDA mean portion size data and the MRCA 90th percentile frequency of eating data, as explained in Exhibit 48. [Note: To obtain the high values, the Subcommittee used the USDA mean and the MRCA 90th percentile data, rather than the reverse, because it was believed that extremes in frequency of eating influence food consumption to a greater extent than do variations in portion size of the food consumed. The use of both the USDA and MRCA 90th percentile values was rejected because of the bizarre and completely unrealistic consumption values obtained with this combination.]
- Both mean and high food consumption values were computed for individuals in each of four age ranges: 0-5 months, 6-11 months, 12-23 months, and 2-65+ years.
- In calculating the consumption values, the MRCA frequency of eating data for both "total sample" (Exhibits 34 and 36) and "eaters only" (Exhibits 35 and 37) were used.
- The mean and 90th percentile frequency of eating values for "total sample" (Exhibits 34 and 36), for each of the age groups within any particular food category, were based on the eating habits of all persons in the respective group, whether or not they consumed any foods in that category during the 14-day MRCA survey period.

- The "eaters only" values (Exhibits 35 and 37), however, were based on the eating habits of only those individuals who ate foods in the particular food category one or more times during the 14-day survey period.
- The intake data in Table 13, Parts A and B (total sample), which are based on the amounts of food consumed by the entire survey population as a whole (Exhibits 42-44), thus represent possible per capita intakes; as such, the intakes for each substance apply not only per individual food category but also for all food categories combined (i.e., the total dietary).
- In contrast, the intakes in Tables 14 and 15 (eaters only), which are based on the amounts of food consumed by persons who regularly eat foods in the respective categories, are valid for any particular substance on an individual food category basis only. They are not cumulative across all food categories, since no person could be expected to eat foods from all categories in any single day at the consumption levels shown in Exhibits 45-47 (eaters only).

Table 13, Parts A and B (total sample)

The intakes for all NAS Appendix A and FEMA questionnaire substances on which usage levels were reported by user firms are presented in Table 13, Part A (substances in Groups I and II) and Part B (substances in Group III). For each substance, intakes are shown for each food category and for all categories combined (total dietary). Intakes were calculated for persons in each of the four age ranges at three different levels: average, high A, and high B.

As explained in Exhibit 54, average intakes were derived from the usual usage levels and mean food consumption values; high A from the usual usage levels and high food consumption values; and high B from the maximum usage levels and mean food consumption values. The significance of these different levels of intake in evaluating the safety of the substances is discussed in Chapter XI.

Table 14, Parts A and B (eaters only)

The two parts of this table are somewhat analogous to those in Table 13, inasmuch as they include data on the same groups of substances, respectively. However, these intakes are based on food consumption by eaters only (i.e., persons who regularly eat foods in these categories) and therefore are applicable on an individual food category basis only (not for all categories combined for any particular substance.) For this reason, the data have been arranged by food category, rather than by substance. This table also differs from Table 13 in that intakes at the very high level (derived from maximum usage levels and high food consumption) have been included. The significance of these data is discussed in Chapter XI.

[Note: These very high values are levels of intake for any particular food category at least theoretically and perhaps practically attainable by a person who ingests food at the "high" consumption level (Exhibits 46 and 47, eaters only) of the category everyday, and if all foods in that category incorporate the GRAS substance, without processing losses, at the maximum levels of use. While perhaps attainable for one or a few categories, no person would be expected to consume all foods in each category at the "high" consumption levels (as much as 9000 calories per day). Furthermore, it would be impossible for any person to select only those foods that incorporate the substance at the maximum level and to consume all such foods in each category at the "high" consumption level. For this reason, very high intakes are provided in Table 14 (eaters only) on an individual food category basis to show potential intake within a particular food category only, but they have not been included in Table 13 (total sample) in which the intakes for all categories are summed to obtain the total dietary intake.]

Table 15 (eaters only)

This table is in the same format as Table 14, since the intakes are based on food consumption by eaters only. The substances (Group IV) in this table are those on which additional questionnaires were reported to NAS and FEMA, i.e., they were not listed in NAS Appendix A or in the FEMA questionnaire. [Note: Because of the small number of usage level reports received on these substances, intakes were not calculated on the basis of food consumption by the total sample, as in Table 13.] The significance of these data is discussed in Chapter XI.

Table 16 (total sample)

This table presents the average total dietary intakes (intakes for all food categories combined) of the substances in Table 13, Parts A and B, in rank order, with the intakes for each of the four age groups listed separately.

[Note: Usage levels as low as 0.00001% were processed from the NAS data, and as low as 0.000001 part per million (0.0000000001%) from the FEMA data. Consequently, a seemingly large number of digits to the right of the decimal point was required in order to show the intakes of those substances used at such low levels in foods consumed in low amounts. For simplicity in programming, all intakes were calculated to the same number of digits, although in most cases the data in Tables 13-16 are not as precise as the number of digits indicated would imply.]

XI. SIGNIFICANCE AND USE OF DATA IN SAFETY EVALUATIONS

Because of certain unavoidable factors inherent in the methods by which intakes were estimated, the Subcommittee believes that the predominant caveat to be observed in the safety evaluations is that the intakes in most cases are overstated, often by considerable margins. Such factors, which have been mentioned in earlier chapters, are listed below:

- In calculating the intakes, it was assumed that each substance is added to all products in each food category in which its use was reported, but this is likely to be the case for only a few substances. (For example, substance X is used in a specialty cracker, but it is probably not used in all, if any, of the other products in the baked goods category.)
- The use of many substances in any given food category was reported by a small number of firms (often only one or two firms out of the total of more than 600 respondents), and hence could not apply to all food products produced in that food category. The usage levels reported by these firms, however, counted as much as if they had been reported by 20 or 100 firms.
- Some substances are lost or altered during processing and/or storage and do not survive into the final foods at the levels of addition. The intakes for such substances may therefore be greatly overstated.
- Some substances are used at relatively high levels as the major component of certain specialty food products, but such uses (and the respective intakes derived therefrom) are not indicative of the concentrations of these substances occurring in foods in general.

Because of these and other factors, the <u>average</u> estimated total dietary intakes as shown in Table 13, Parts A and B, are likely to be much higher than would be the intakes achieved through consumption of a diet

consisting totally of processed foods to which the substances had been added at the maximum levels. The high A and high B levels of intake, based on extremes in food consumption and levels of use, respectively, represent intakes even further from those to be expected in the average consumer. These high intakes could only and rarely be achieved in certain persons through consumption of foods at a frequency of eating greater than that of 90 percent of the population (high A) or through careful selection and consumption of foods to which the substances were known to have been added at the maximum levels (high B).

The intakes in Table 14, Parts A and B, and in Table 15 (all on an individual food category basis) could be achieved for any one food category if the foods selected contained the levels of the substances shown in Tables 2-5 and if they were consumed at the levels shown in Exhibits 45-47 (eaters only). It is not likely, however, that foods from more than a few such categories could be selected and eaten in any single day or even during an extended period of time. To achieve the very high intakes in any particular food category, the consumer would have to select a food to which the GRAS substance had been added at the maximum level and in addition would also have to consume the food at a frequency of eating greater than that of 90 percent of the population.

One way in which the intakes reported in Table 13, Parts A and B, may be evaluated is through comparison of per capita intakes based on the annual poundage data shown in Table 11. As indicated in Chapter X, the Subcommittee estimated that the annual poundage data reported by all respondents represent, on the average, between 60 and 70% of the actual poundage of the substances added to the nation's food supply annually. Even if the lower figure of 60% were used, it could be shown (by applying appropriate conversion factors and assuming a total U.S. population of 200,000,000 persons) that the average total dietary intake values in Table 13, Parts A and B, are from several times to thousands of times greater than are those calculated on a per capita basis from the annual poundage data. Such calculations have been made on a number of GRAS substances as shown in Exhibit 58. The substances selected were among those for which acceptable daily intakes (ADI's) have been developed by the FAO-WHO Joint Expert Committee on Food Additives. For comparative purposes, daily intakes

calculated from the ADI's are shown in Exhibit 58 in relation to the intakes from Table 13 and those calculated from the annual poundage data. [Note: The values in Exhibit 58 tend to indicate that the ratio of intakes from Table 13 to those calculated from the annual poundage data (i.e., the NAS # 1 to NAS # 2 ratio) increases as the number of firms reporting per food category decreases. For example, the ratio for potassium metabisulfite is only 1.1 (11 firms per category), whereas that for methylparaben is 2460 (1 firm per category).]

* * * *

It should be noted that none of the intakes in this report include any amounts of the substances that may be ingested from sources other than foods to which the substances have been intentionally added. Therefore, in the evaluations of safety, potential intakes contributed by foods in which the substances occur naturally, by pharmaceuticals, by drinking water, and by agricultural uses and other environmental factors should be taken into account.

* * * *

Finally, it should be emphasized that the Subcommittee's task has not been to evaluate the safety of use of the substances reported herein. In those cases where the Subcommittee has pointed out certain unavoidable aspects of the survey method and procedures that tend to overstate the usage levels and daily intakes, this has been done in an attempt to call attention to those areas in which such values, in relation to the overall data reported, may require special consideration.

XII. RECOMMENDATIONS

The Subcommittee offers the following recommendations for consideration by FDA and the expert panels making the safety evaluations:

- In order to conduct a more accurate survey on the intake of substances used in food processing, food consumption data collected specifically for this purpose are needed.
- Better and more detailed information than is now available on food consumption is required in order to more clearly establish dietary patterns of the population as a whole, and especially for the aged, the very young, individuals under medical stress situations, pregnant and lactating women, the poor, and ethnic minorities.
- Surveys on the occurrence and use of substances in the nation's food supply should be conducted frequently and be kept current with changing food consumption patterns that develop upon the introduction of newer foods, some of which may partially replace certain foods now in use.
- More accurate data on intakes will also require much more information on processing losses, interreactions, and other factors that alter the amount or identity of the added substance as it ultimately occurs in the food at the time of consumption. This will often require actual analysis of the foods as consumed.
- When questions or uncertainties arise during the safety evaluations, outside experts (either academic or industrial scientists and technologists) should be consulted, as necessary, to supplement the information provided herein.

XIII. SUMMARY AND CONCLUSIONS

The documents and procedures employed in a comprehensive survey on the use of GRAS substances have been described, the data obtained in the survey have been summarized, and comments on the manner in which the data should be interpreted during safety evaluations have been provided.

The Subcommittee has found that the usage levels reported by the survey respondents, with certain exceptions, appear to be reasonably accurate and are indicative of the levels of the substances currently being added to foods processed in the United States. Because of certain unavoidable aspects of the methods by which the usage level data were reported and utilized, the daily intakes calculated from the usage levels and food consumption data tend to be overstated, often by considerable margins.

The Subcommittee has made certain recommendations regarding the need for data on food consumption designed specifically for use in future surveys, which should be conducted at frequent intervals.

XIV. LIST OF EXHIBITS

32. (A) Description of MRCA Menu Census; (B) Description of USDA Survey
33. (A) Correlation and Revision of Food Categories for Use with MRCA, USDA, and Usage Level Data in Computing Food Consumption and GRAS Intakes; (B) MRCA Codes for Regular Foods; (C) MRCA Codes for Infant Formula Products and Baby Foods
34. MRCA Frequency of Eating of Regular Foods by Males + Females in Different Age Groups, Total Sample
35. MRCA Frequency of Eating of Regular Foods by Males + Females in Different Age Groups, Eaters Only
36. MRCA Frequency of Eating of Infant Formula Products and Baby Foods by Males + Females, 0-23 Months, Total Sample
37. MRCA Frequency of Eating of Infant Formula Products and Baby Foods by Males + Females, 0-23 Months, Eaters Only
38. Explanatory Notes on Exhibits 34-37 (MRCA Data)
39. USDA Mean Portion Sizes of Regular Foods Consumed by Males + Females in Different Age Groups
40. USDA Mean Portion Sizes of Infant Formula Products and Baby Foods Consumed by Males + Females, 0-23 Months
41. Explanatory Notes on Exhibits 39 and 40 (USDA Data)
42. Consumption of Regular Foods by Males + Females, 2-65+ Years, Total Sample
43. Consumption of Regular Foods by Males + Females, 0-23 Months, Total Sample
44. Consumption of Infant Formula Products and Baby Foods by Males + Females, 0-23 Months, Total Sample
45. Consumption of Regular Foods by Males + Females, 2-65+ Years, Eaters Only
46. Consumption of Regular Foods by Males + Females, 0-23 Months, Eaters Only
47. Consumption of Infant Formula Products and Baby Foods by Males + Females, 0-23 Months, Eaters Only
48. Explanatory Notes on Exhibits 42-47 (Food Consumption Calculations)
49. Explanatory Notes on Table 1 (Reports Submitted on Survey Substances)
50. Explanatory Notes on Tables 2-5 (Usage Levels)
51. Explanatory Notes on Tables 6-10 (Technical Effects and Importance Rating)
52. Explanatory Notes on Table 11 (Annual Poundage)
53. Explanatory Notes on Table 12 (Year of First Use)
54. Explanatory Notes on Table 13 (Possible Daily Intakes, Total Dietary--Total Sample)
55. Explanatory Notes on Tables 14 and 15 (Potential Daily Intakes Per Food Category--Eaters Only)
56. Explanatory Notes on Table 16 (Substances Ranked by Possible Average Daily Intake)
57. Comments on Use of GRAS Substances in Brewing of Malt Beverages Submitted by USBA.
58. Comparison of Intakes

XV. ACKNOWLEDGMENTS

The Subcommittee expresses its appreciation to the following for providing valuable assistance in various phases of the project:

- U.S. Department of Agriculture, Agricultural Research Service, for providing a tape of data obtained in the 1965 food intake survey.
- The Flavor and Extract Manufacturers' Association, for providing data from the survey on flavoring ingredients and adjuncts.
- The National Association of Chewing Gum Manufacturers, for providing data from the subsurvey on chewing gum.
- The National Confectioners Scientific and Educational Foundation, for providing data from the subsurvey on highly flavored candy.
- The 20 industrial associations (see Exhibit 22), for providing membership lists used in the development of the questionnaire mailing lists.
- The NAS Office of Scientific Personnel, for handling all phases of data processing and programming.

In addition, the Subcommittee expresses its thanks to the following for expert services rendered: Mr. Edwin Bridgforth, Subcommittee consultant on food consumption statistics; Dr. George Harris, pilot phase consultant on questionnaire design, Arthur D. Little, Inc.; and Mr. Alan Dordek and Mr. Edward Mozes, Market Research Corporation of America.